IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT :	CALLEGARO et al.	EXAMINER :	FUBARA, B.M.
SERIAL NO. :	09/743,333	ART UNIT :	1618
FILED :	February 21, 2001	CONFIRM NO.:	9321

FOR BIOCOMPATIBLE AND BIODEGRADABLE COMPOSITIONS CONTAINING HYALURONIC ACID AND THE DERIVATIVES THEREOF FOR THE TREATMENT OF ULCERS IN THE DIGESTIVE APPARATUS

May 21, 2010

BRIEF ON APPEAL

Mail Stop – Board of Patent Appeals and Interferences
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action of June 25, 2009, the claims having been twice rejected, a Notice of Appeal was filed on December 24, 2009. Appellant submits herewith a Brief on Appeal in support of an appeal of the rejection of claims 25 – 32 and 34 – 51 by the Examiner.

Please charge the fee for filing the Brief on Appeal for large entity of $540.00 to our Deposit Account No. 01-0035.

Also enclosed herewith is a Petition for an Extension of Time for a Large Entity in the amount of $1,110.00. The $1100.00 payment should also be charged to our Deposit Account No. 01-0035.

The USPTO is authorized to charge any additional fees which may be required or credit any overpayment to Deposit Account No. 01-0035.

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(i.) REAL PARTY IN INTEREST

Fidia Advanced Biopolymers, S. r. L., is the real party in interest, and is the assignee of Application 09/743,333.

(ii.) RELATED APPEALS AND INTERFERENCES

On April 16, 2007, the Board of Patent Appeals and Interferences affirmed the rejection under 35 USC § 103(a) of claims 25, 26- 32 and 34 – 44.

A copy of that Decision by the Board is attached hereto as Appendix X as required by 37 CFR 41.37(c)(1)(x).

(iii.) STATUS OF CLAIMS

The claims pending in the Application are 25 – 32 and 34 – 51.

Claims 25 – 32 and 34 – 51 stand rejected under 35 USC §112, first paragraph.

Claims 25 – 32 and 34 – 51 stand rejected under 35 USC § 112, second paragraph.

Claims 25 – 32 and 34 – 51 stand rejected under 35 USC § 103(a).

(iv.) STATUS OF AMENDMENTS

A PRE-APPEAL BRIEF REQUEST FOR REVIEW was filed on December 24, 2009. A Notice of Panel Decision from Pre-Appeal Brief Review of February 23, 2010 determined that it was an Improper Request since the pre-appeal was more than five (5) pages in total.

The Amendment of April 1, 2009 was the last-filed Amendment.

(v.) SUMMARY OF THE CLAIMED SUBJECT MATTER

When reference is made hereinafter to pages of the publication, it is to International Application No. WO 00/01394.

Independent claim 25 recites a process for preparing a biological material for the treatment of lesions and ulcers of the gastrointestinal system (pg. 2, lines 31-33) (pg. 3, lines 1-7, 13-15) which includes the seeding and growing of enterocytes (pg. 6, lines 7-9), optionally in the presence of other cells (pg. 5, lines 23-27), on either a bidimensional perforated membrane or on a bidimensional continuous membrane (pg 5, lines 11 and 23). The bidimensional perforated membrane or the bidimensional continuous membrane upon which the enterocytes are seeded and grown consists of hyaluronic acid or a derivative of hyaluronic acid (pg.3, lines 13-15 and pg. 4, lines 7-31), obtaining as a result of the process morphologically differentiated enterocytes (pg. 6, lines 7-9, pg. 7, lines 1-3) the differentiation being confirmed by the presence of microvilli. (Pg.7, lines 8-11).

Dependent process claim 26 specifies that the hyaluronic acid derivatives are esters wherein the carboxy function is esterified with aliphatic, aromatic, arylaliphatic, cycloaliphatic or heterocyclic alcohols (pg.4, lines 7-11).

Dependent process claim 27 specifies that the hyaluronic acid (HA) derivatives are cross-linked esters of hyaluronic acid wherein the carboxy groups are esterified with alcoholic functions of the same polysaccharide chain or other chains (pg. 4, lines 12-14).

Dependent process claim 28 specifies that the HA derivatives are cross-linked esters of HA wherein the carboxy groups are esterified with polyalcohols of the aliphatic, aromatic

arylaliphatic, cycloatiphatic or heterocyclic series, generating cross-linking by spacer chains (pg. 4, lines 15-18).

Dependant process claim 29 specifies that the HA derivatives are hemiesters of succinic acid or the heavy metal salts thereof with HA or with partial or total esters of HA (pg.4, lines 19-23).

Dependant process claim 30 specifies that HA dervivatives are O-sulphated or N-sulphated derivatives (pg. 4, lines 22-24).

Dependent process claim 31 specifies that the HA derivatives are amides wherein the free carboxyls of HA are reacted with primary or secondary aliphatic, aromatic, arylaliphatic cycloaliphatics or heterocyclic amines, that optionally can be pharmaceutically active (pg. 4, lines 25-28).

Dependent process claim 32 specifies an HA derivative which is an amide having a deacetylated amino group of HA or an HA ester wherein the carboxy function is esterified with an aliphatic, aromatic, arylaliphatic cycloaliphatic or heterocyclic alcohol. (Pg. 4, lines 11-14 and 28-31).

Claim 34 depends from dependent process claim 26 and it specifies a biological material for the treatment of lesions and ulcers of the gastrointestinal system (pg. 2, lines 1-3 and 31-33 and pg. 3, lines 13-15) which includes enterocytes (pg. 6, lines 7-9) which are morphologically differentiated as evidenced by the formation of microvilli (pg. 7, lines 11-13) with other optional cells (pg. 5, lines 23-27) on a bidimensional continuous membrane (pg. 5, line 11), the membrane consisting of at least one HA derivative (pg. 5, lines 23-25).

Claim 35, 36, 37 and 38 are all process claims which depend from independent process 25 and specify reactions which are disclosed at page 4, lines 7-31.

Dependent claims 39-44, respectively, are biological material claims which depend from process claims 27-32, respectively, in the same manner as heretofore described biological material claim 34 depends from process claim 26, wherein the enterocytes (pg. 6, lines 7-9, pg. 7, lines 1 – 4) are formed on a bidimensional continuous membrane of HA or a derivative thereof (pg. 5, lines 23-25).

Dependant claims 45-51, respectively are biological material claims which depend from process claims 26-32, respectively wherein the enterocytes (pg. 6, lines 7-9 and pg. 7, lines 1-4) are formed on a bidimensional perforated membrane of HA or a derivative thereof (pg. 5, line 11; pg. 3, lines 13-15).

vi. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 25 – 32 and 34 – 51 stand rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. The claims are said by the Examiner to contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention.

Claims 25 – 32 and 34 – 51 stand rejected under 35 USC § 112 , second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Examiner the boundaries for the protection sought for derivatives of hyaluronic acid as recited in the claims are not discernible making the scope of the claims unclear and indefinite.

Claims 25 – 32 and 34 – 51 stand rejected under 35 USC § 103(a) as being unpatentable over Valentini et al. (US 5, 939,323).

Claims 25 – 32 and 34 – 51 stand rejected under 35 USC § 103(a) as being unpatentable over Dorigatti et al. (WO 94/17837) in view of Valentini et al. (US 5,939,323).

Claims 25 - 32 and 34 – 51 stand rejected under 35 USC § 103(a) as being unpatentable over Soranzo (WO96/35750) in view of Valentini et al. (US 5,939,323).

vii. ARGUMENT

1. Rejection Under 35 USC §112, First Paragraph, of Claims 25 – 32 and 34 - 51

According to the Office Action of June 25, 2009, at page 3, paragraph 5, the Examiner states, "The amended claims have recited seeding and growing enterocytes. But the specification as filed does not envision seeding enterocytes."

Appellants disagree with this conclusion since, indeed, enterocytes are well supported in the as-filed application, for example, at page 6, lines 7-9 and page 7, lines 1-4. Furthermore, it is well known to one of ordinary skill in the art that intestinal cells spontaneously differentiate into enterocytes, which are typical of the mature intestinal epithelium.

However, it should be noted that in the Office Action dated October 1, 2008, at page 7 thereof, with reference to the Declaration submitted by Anna Zanellato, the Examiner asserted that the pending claims recited "generic intestinal cells and not enterocytes". Therefore, Appellants decided to follow the Examiner's indication by substituting "enterocytes" in claim 25 for "intestinal cells", even though the meaning of the first expression was preferable to Appellants, being that ***enterocytes*** are indeed intestinal absorptive cells.

Therefore, the new matter rejection under Section 112, first paragraph is clearly improper and should be reversed.

2. Rejection Under 35 USC § 112, Second Paragraph of Claims 25 – 32 and 34 – 51

The Examiner maintains that the pending claims are indefinite for failing to particularly point out the boundaries of the protection sought for the hyaluronic acid (HA) derivatives.

Appellants disagree with this conclusion since according to MPEP §2111, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." (See the Federal Circuit's en banc decision in Phillips v. AWH Corp., 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005)). In this case, the HA derivatives are clearly defined at page 4, lines 6-31. Therefore, the broadest reasonable interpretation of the claims is consistent with the interpretation that those skilled in the art would reach (see *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999)), because the skilled person can readily, and would undoubtedly, refer to the list provided in the specification in order to understand the scope of the expression "*HA derivative*".

It should be noted that the Examiner never raised this rejection previously, even though the expression has been present since the filing of the application.

Therefore, the rejection for indefiniteness under 35 USC § 112, second paragraph, is also clearly improper and should be reversed.

3. Rejection under 35 U.S.C. §103(a) as being obvious over Valentini et al. (US 5,939,323)

The Examiner states at p. 4, item 12 of the June 25, 2009 Office Action that

> "Valentini et al. describes that derivatives of hyaluronic acid are employed as raw material to fabricate porous, degradable scaffolds for medical purposes such as tissue repair and reconstruction and wound healing" (Col 1., lines 64 – 67) and that "specifically discloses that the scaffolds can have virtually any size, thickness and shape having various porosities and pore size" (column 4, lines 36-38).

Furthermore, the Examiner states that "scaffolds can be seeded with cells such as … intestinal cells" (column 8, lines 1-6).

Thus, the Examiner concludes that

"the perforated membrane of the claims read on the porous scaffold of Valentini, which scaffold can also be a membrane", while acknowledging that Valentini does not disclose a 2-D matrix. (Page 6, 2nd full paragraph, line 3)

The Examiner then adds that

> "taking the general teaching of Valentini as regards the design and use of scaffold of any shape and structure and size, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that intestinal cells seeded on the 3-D matrix or any other structural matrix including 2-D matrix or continuous matrix will grow. The prior art and the claimed invention achieve the same result of growing intestinal cells on hyaluronic acid matrix. There is no demonstration that intestinal cells cannot be seeded on the 3-D matrix of Valentini." (Pages 6 – 7 of June 25, 2009 Office Action)

Moreover, the Examiner, in responding to Appellants' previous arguments, stated that "the language of perforated does not exclude the porous structure of Valentini and, basically, a perforated membrane is porous" and that "neither Annex 1, Annex 2 nor Annex 3 categorically states that a perforated material is non-porous".

By contrast, in Appellants' view, the Examiner has ***arbitrarily isolated*** sentences from Valentini et al. in order to conveniently lead to the claimed invention. This represents a clear case of hindsight reconstruction of the claimed invention. As the CAFC said in the Gorman case, "It is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gap." (In re Gorman, 18 USPQ, 2d, 1885 Fed. Cir. 1991).

As a matter of fact, Valentini et al. at column 4, lines 30-38, teach that:

> The invention involves three-dimensional biodegradable scaffolds of hyaluronic acid derivatives for tissue reconstruction and repair. The porous scaffold has interconnected pores that permit cells to grow into the scaffold, preferably completely penetrating the scaffold with cells and thereby eventually replacing the scaffold with tissue. The scaffold can be fabricated to be virtually any shape, size or thickness, and can be produced to various porosities and pore sizes,

depending upon the application. The scaffold is degradable, so that it can eventually be replaced by tissue.

Therefore, the sentence where "the scaffolds can have virtually any size, thickness and shape having various porosities and pore size" is expressly and unambiguously referring to the three-dimensional scaffolds of the immediately preceding sentence in the same paragraph. This is abundantly clear when considering the later statement at lines 45-46 where it is specified that "void volumes can range from 40-90% of the scaffolds".

Thus, one of ordinary skill in the art reading this patent is no doubt aware of the fact that Valentini et al. ***only refer to 3-D scaffolds***, even more so in view of the fact that the required pores, i.e. void volumes, are ***unambiguously 3-D cavities***.

The Examiner states that Valentini et al. suggest that the scaffold can be a bidimensional membrane, in view of the fact that the patent discloses placing the scaffold on a membrane insert!

Appellants wonder why the person of ordinary skill would have read this in the manner posited by the Examiner. Again, Appellants are convinced that this is the result of an ***ex post facto analysis*** made by the Examiner having derived her knowledge solely from the claimed invention.

Indeed, the skilled person would never have misinterpreted this prior art document as has surprisingly been done by the Examiner. As a matter of fact, Valentini et al. expressly and unambiguously teach as follows:

1) the scaffolds must be "a three dimensional structure of interconnected pores which permits cell ingrowth and, eventually, tissue replacement of the scaffold" (column 2, lines 54-56);

2) the method for forming said scaffolds requires the use of a pore forming agent;

3) "In one particularly preferred embodiment, the pore forming agent is particles having a diameter between 10-1000 μm with optimal tissue ingrowth at 106 and 600 μm" (column 2, lines 56-59);

4) pores are void volumes in the scaffolds (column 4, lines 45-47).

From the above essential features, it is evident that the skilled person is taught to always configure a 3-D scaffold having interconnected pores where the ingrowth of cells takes place in order to succeed in repairing damage, including damage to visceral organs.

The requirement of a 3-D scaffold is even more evident when considering that the pores are 3-D cavities that must be present in said scaffolds. Therefore, when Valentini et al. refer to the possibility to have any shape and structure and size, this is always to be understood ***as any shape and structure and size of 3-D scaffolds having interconnected pores***.

Now, Appellants wonder how would the skilled person be motivated to modify the teaching of Valentini et al. in the direction of the claimed invention, ***when all of the requirements needed by the Valentini et al. scaffolds teach away from the claimed invention*** and when the Examiner has acknowledged that Valentini does not disclose a 2-D matrix? As the CAFC held in Bausch & Lomb, Inc. v. Barnes Hind Hydrocurve Inc., 230 USPQ 416 (Fed.Cir. 1986) a reference should be considered as a whole, and ***portions arguing against or teaching away from the claimed invention must be considered.***

Even more so, how would the ordinary skilled person possibly consider a 2-D matrix, when he/she is taught to necessarily have a porous structure and the pores are unambiguously known to be 3-D cavities, i.e. void volumes?

In this regard, how can the Examiner possibly state that "the perforated 2-D membrane reads on the porous 3-D scaffold of Valentini", without acknowledging that this is an evident instance of hindsight?

As reported above, the Examiner states that "the language of perforated does not exclude the porous structure of Valentini and, basically, a perforated membrane is porous" and that "neither Annex 1, Annex 2 nor Annex 3 categorically states that a perforated material is non-porous". This assertion is ***absolutely contradictory*** since a bidimensional membrane necessarily does not possess the physical possibility of being porous, ***as the third dimension is negligible by definition***! Therefore, how can it be that bidimensional openings in a bidimensional perforated membrane (see Annex 5 attached to the May 12, 2008 amendment) read on pores, when it is commonly known that pores are 3-D cavities?

It is clear that the expectation of success indeed falls flat when the teaching of Valentini et al. is not followed, i.e. when no porosity on a necessarily 3-D scaffold is provided, also in the case of intestinal cells. Thus, how could the skilled person, at the time the invention was made, believe he/she would succeed in growing enterocytes on a bidimensional membrane that necessarily does not have the physical possibility of being porous, as the third dimension is negligible by definition, and thus does not and cannot provide the cavities where the ingrowth of cells could take place?

As a matter of fact, the claimed biological material comprises the bidimensional membrane allowing the enterocytes to grow only bidimensionally and this is not possible with

the porous 3-D scaffold of Valentini et al., wherein the cells are taught to grow within the suitably provided pores.

Furthermore, the Examiner states that the Declaration of Mrs. Anna Zanellato (filed April 12, 2009) is not commensurate with the claims since specific cells derived from $CaCO_2$ cell lines were used and not enterocytes.

This statement by the Examiner is definitely groundless, since the skilled person at the time the invention was made clearly knew that said cell line derives from intestinal tumors and are commonly used in *in vitro* assays to predict the absorption rate of candidate drug compounds across the intestinal epithelial cell barrier, as is explained fully at page 6, lines 7-9, of the instant specification.

Therefore, all of the results set forth in Mrs. Zanellato's Declaration are proper and further demonstrate that the claimed combination of features is neither suggested nor motivated at all by the teaching of Valentini et al.

Thus, for at least the above reasons, the claims clearly distinguish over Valentini et al. and the § 103(a) obviousness rejection should be reversed since the Examiner has not established a case of *prima facie* obviousness by a preponderance of the evidence.

4. Rejection of claims 25 – 32 and 34 – 51 under 35 U.S.C. §103(a) as being obvious over Valentini et al. (US 5,939,323) in view of Dorigatti et al. (WO 94/17837)

Dorigatti et al. disclose multilayer non-woven tissues having a minimum of 2 to 4 layers, wherein a layer that comes into contact with the skin is made of a hyaluronic acid derivative. These multilayer non-woven tissues are used in dermatology, "in medical/pharmaceutical field to cover the skin" (page 6, lines 2 - 6), thus they are used for external purposes.

Appellants, therefore, wonder why the skilled person would have even contemplated the possibility of combining Valentini et al. with Dorigatti et al., when the latter clearly does not pertain to the field of endeavour of the claimed invention, and even why the hypothetical combination of the teaching of a 3-D scaffold having interconnected pores and the teaching of multilayer non-woven tissues would result in a bidimensional membrane!

And also, even arbitrarily decontextualizing the information as the Examiner does, thus considering the sole hyaluronic acid derivative layer used in Dorigatti et al., it is disclosed that the same is non-woven, but nowhere in the document is it specified that said layer is and/or must be a ***bidimensional non-woven layer***, so that the cells are ***grown only bidimensionally***.

Appellants are definitely convinced that the Examiner has once again come to her conclusion on the basis of a further hindsight, while it is clear to Appellants that the skilled person would have had no reason to take Dorigatti et al., which is a non-analogous secondary reference, into consideration, nor even to combine the same with Valentini et al. in order to achieve the claimed invention. In re Oetiker, 24 USPQ, 2d 1443 (Fed.Cir. 1992)

Therefore, Appellants emphatically disagree with the Examiner, who affirmed, at page 12, par. 25, of the June 25, 2009 Office Action, that:

> In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning.

It is evident that the Examiner has, indeed, gone well beyond the actual disclosure of the prior art documents in order to arrive at the claimed invention having derived her knowledge of the claimed invention solely from Appellants' disclosure.

Thus, since the defects and deficiencies of the primary reference to Valentini et al. have not, in any manner, been remedied by the secondary reference to Dorigatti et al., for at least the above reasons, the obviousness rejection has clearly been overcome and should be reversed.

5. Rejection of claims 25 – 32 and 34 – 51 under 35 U.S.C. §103(a) as being obvious over Valentini et al. (US 5,939,323) in view of Soranzo et al. (WO 96/33750)

Soranzo et al. disclose "artificial human skin comprising:

a) a microperforated membrane based on a hyaluronic acid derivative, on which keranocytes have been seeded and cultured,

b) an underlying non-woven tissue based on a hyaluronic acid derivative wherein fibroblasts have been seeded and left to proliferate" (see Claim 1)

that is used in dermatology, as a dermo-epidermal junction, in diagnostics, in the cosmetic field, for instance in hair grafting; in sum, for external purposes only.

Soranzo's artificial human skin is deemed to meet the following requirements, as listed at page 3, lines 3-11:

> "1) their surfaces must allow for adhesion and cell growth;
>
> 2) neither the polymers themselves, nor their degradation products should cause inflammation or toxic phenomena when implanted *in vivo*;
>
> 3) the product should be perfectly reproducible in its three dimensions;
>
> 4) its ideal porosity is 50%, which gives a large surface area for cell-polymer interactions, sufficient volume for the deposit of extracellular matrix and only slight, or no, migrational impediments during *in vitro* culture."

Therefore, the teaching of Soranzo et al. taken ***as a whole*** is definitely different and readily distinguishable from the very particular teaching of Soranzo et al. employed by the Examiner which, once again, has arbitrarily been decontextualized by the Examiner. As a matter of fact, once again, ***the cell growth is taught to require three dimensional matrixes having a***

porosity of preferably 50%, so that a perfectly functional dermo-epidermal junction is obtained (page 4, lines 8, and page 5, lines 5-10).

Therefore, even in this case, Appellants wonder why the ordinary skilled person would have even contemplated combining Valentini et al. with Soranzo et al., when the latter clearly does not pertain to the field of endeavour of the claimed invention, and even why the hypothetical combination of the teaching of a 3-D scaffold having interconnected pores and the teaching of artificial human skin where the fibroblasts are grown on 3-D non-woven tissue, would ***result in a bidimensional membrane!***

The Examiner deems Soranzo et al. to be a relevant document since Laserskin® is used as microperforated membrane in the artificial human skin. However, it should be noted as follows:

1- the microperforated membrane of Soranzo et al. is not used as such, but is ***always coupled*** with a 3-D non-woven tissue to form the final product to be used for ***external purposes***;

2- keratocytes are grown on said membrane, whereas fibroblasts are grown on the 3-D non-woven tissue; and,

3- all of the requirements/advantages which the final product must meet are only ascribable to the 3-D structure, as indicated above.

Therefore, why would the skilled person have been motivated to take the teaching of Sorzano et al. into consideration, as it does not even pertain to the field of endeavour of the claimed invention? And, furthermore, where is there even a suggestion to combine the two documents, when both the teachings, either alone or taken together, are expressly and exclusively focused in the direction of 3-D structures?

In view of the above, Appellants are absolutely eonvineed that the Examiner once again has come to her eonelusions on the basis of a further hindsight, while it is elear that the skilled person would have had no reason to take Soranzo et al. into consideration, nor even to combine the same with Valentini et al. in order to arrive at the claimed invention.

Thus, sinee the defeets and defieieneies of the primary referenee to Valentini et al. have not been remedied by the teaehings of the seeondary referenee to Soranzo et al., for at least the above reasons, the obviousness rejeetion should be reversed, sinee *prima facie* obviousness has not been established by a preponderanee of the evidenee.

CONCLUSION

In view of the foregoing arguments as supplemented by the reeord herein, the rejeetions under 35 USC § 112, first and seeond paragraphs, of elaims 25 – 32 and 34 – 51 have been overcome and should be reversed.

Similarly, elaims 25 -32 and 34 – 51 elearly distinguish over the art of reeord and the three (3) 35 USC § 103(a) rejeetions having been overeome by a preponderance of the evidenee, the rejections should be reversed and the Examiner should be direeted to issue a Notice of Allowanee.

Respectfully submitted,

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(viii). CLAIMS APPENDIX

25. A process for the preparation of a biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus, which comprises seeding and growing enterocytes optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells on a bidimensional perforated membrane or on a bidimensional continuous membrane consisting essentially of at least one hyaluronic acid or a derivative thereof thereby obtaining morphologically differentiated enterocytes as confirmed by the presence of microvilli.

26. The process according to claim 25, wherein the said hyaluronic acid derivatives are hyaluronic acid esters whercin part or all of the carboxy functions are esterified with alcohols of the aliphatic, aromatic, arylaliphatic, cycloaliphatic, heterocyclic series.

27. The process according to claim 25, wherein the said hyaluronic acid derivatives are the cross-linked esters of hyaluronic acid wherein part or all of the carboxy groups are esterified with the alcoholic functions of the same polysaccharide chain or other chains.

28. The process according to claim 25, wherein thc said hyaluronic acid derivatives are the cross-linked compounds of hyaluronic acid wherein part or all of the carboxy groups are estcrified with polyalcohols of the aliphatic, aromatic, arylaliphatic, cycloaliphatic, heterocyclic series, generating cross-linking by means of spacer chains.

29. The process according to claim 25, wherein the said hyaluronic acid derivatives are hemiesters of succinic acid or heavy metal salts of the hemiester of succinic acid with hyaluronic acid or partial or total csters of hyaluronic acid.

30. The process according to claim 25, wherein the said hyaluronic acid derivatives are O-sulphated or N-sulphated hyaluronic acid derivatives.

31. The process according to claim 25, wherein the said hyaluronic acid derivatives are hyaluronic acid amides wherein part or all the free carboxylic groups of hyaluronic acid are reacted with a primary or a secondary amine selected from the group consisting of thc aliphatic, aromatic, arylaliphatic, cycloaliphatic or heterocyclic amine, that can optionally be a pharmaceutically active substance.

32. The process according to claim 25, wherein the said hyaluronic acid derivatives are

amides wherein a deacylated amino group of hyaluronic acid or of a hyaluronic acid ester wherein part or all of the carboxy functions are esterified with an alcohol selected from the group consisting of aliphatic, aromatic arylaliphatic, cycloaliphatic and heterocyclic series, is reacted with an acid selected from the group consisting of aliphatic, aromatic, arylaliphatic and cycloaliphatic acid, that can optionally be a pharmaceutically active substance.

34. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional continuous membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 26.

35. The process according to claim 25, wherein the hyaluronic acid derivatives are amides wherein a deacylated amino group of hyaluronic acid or of a cross-linked ester of hyaluronic acid wherein part or all of the carboxy groups are esterified with the alcoholic functions of the same polysaccharide chain or other chains, is reacted with an acid selected from the group consisting of aliphatic, aromatic, arylaliphatic and cycloaliphatic acids, that optionally can be a pharmaceutically active substance.

36. The process according to claim 25, wherein the hyaluronic acid derivatives are amides wherein a deacylated amino group of hyaluronic acid or of a cross-linked compound of hyaluronic acid wherein part or all of the carboxy groups are esterified with polyalcohols of the aliphatic, aromatic, arylaliphatic and cycloaliphatic, and heterocyclic series, generating cross-linking by means of spacer chains, is reacted with an acid selected from the group consisting of the aliphatic, aromatic, arylaliphatic and cycloaliphatic acids, that optionally can be a pharmaceutically active substance.

37. The process according to claim 25, wherein the hyaluronic acid derivatives are amides wherein a deacylated amino group of hyaluronic acid or of a hemiesters of succinic acid or heavy metal salts of the hemiester of succinic acid with hyaluronic acid or partial or total esters of hyaluronic acid, is reacted with an acid selected from the group consisting of aliphatic, aromatic, arylaliphatic and cycloaliphatic acids, that optionally can be a pharmaceutically active substance.

38. The process according to claim 25, wherein the hyaluronic acid derivatives are amides wherein a deacylated amino group of hyaluronic acid or of a O-sulphated or N-sulphated hyaluronic acid derivative, is reacted with an acid selected from the group consisting of aliphatic, aromatic, arylaliphatic and cycloaliphatic acids that optionally can be a pharmaceutically active substance.

39. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblast, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional continuous membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 27.

40. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblast, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional continuous membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 28.

41. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblast, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional continuous membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 29.

42. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblast, mesenchymal cells, mature cells and/or epithelial

cells, on

b) a bidimensional continuous membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 30.

43. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblast, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional continuous membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 31.

44. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblast, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional continuous membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 32.

45. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional perforated membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 26.

46. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional perforated membrane consisting essentially of at least one hyaluronic

acid derivative as defined in claim 27.

47. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional perforated membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 28.

48. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional perforated membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 29.

49. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional perforated membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 30.

50. A biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells, on

b) a bidimensional perforated membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 31.

51. A biological material for the treatment of ulcers, lesions and diverticula of the digestive

and gastrointestinal apparatus comprising:

a) enterocytes morphologically differentiated as confirmed by the presence of microvilli, optionally together with fibroblasts, mesenchymal cells, mature cells and/or epithelial cells, on

a bidimensional perforated membrane consisting essentially of at least one hyaluronic acid derivative as defined in claim 32.

(ix) Evidence appendix

A copy of Anna Zanalleto's Declaration under 37 C.F.R. § 1.132 is attached.

The Declaration was entered in the record by the Examiner in the Office Action of June 25, 2009.

PATENT
ATTORNEY DOCKET NO. 204,940

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Callegaro et al.	Confirmation No.:	9321
Serial No.:	09/743,333	Art Unit:	1618
Filed:	February 21, 2001	Examiner:	Blessing M. Fubara
Title:	"Biocompatible and biodegradable composition containing hyaluronic acid and the derivatives thereof for the treatment of the digestive tract of the ulcers"		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

I, Anna Zanellato, being duly sworn depose and say that:

1. I am an Italian citizen residing at: Bovolenta (PD)

2. I am familiar with the English language.

3. I graduated in: BIOLOGY at the University of Padua in the academic year: 1987

4. I am author of 19 Scientific publications.

5. Previous job experiences: From 1987 to 1990 I had worked at the University Department of General Pathology as a researcher, where I had been involved in a study pertaining to smooth muscles cells cultures and in particular to the mechanism of atherosclerosis.

6. Actual job: Since 1990 I have been working at FIDIA FARMACEUTICI S.p.A. in the field of research, involving:

- the analysis of action mechanism of trophic factors,
- studies, utilizing neuronal cultures to select new chemical molecules pharmacologically active to prevent different types of neuronal pathologies,
- other studies concerning bovine, rabbit, human, articular chondrocytes cultures on the biomaterials comprising and/or consisting of hyaluronic acid derivatives.

The following tests had been carried out under my own responsibility.

Experimental section

Enterocytes ($CaCO_2$ cell line that differentiates into enterocytes typical of the mature intestinal epithelium) were seeded onto supports made of the total benzyl ester of hyaluronic acid in the form of :

- a bidimensional continuous membrane, as shown in Figure A below,
- a bidimensional perforated membrane (Laserskin®), and
- a non-woven 3-D matrix, as shown in Figure B below,

in order to test their biocompatibility, and their morphological and biochemical responses were observed.

Figure A shows the 2-D continuous membrane as raw material for the purposes of the current invention, whereas the perforated membrane is the same 2-D continuous membrane where regularly spaced openings have been made.
Figure B shows a 3-D non-woven matrix made of Hyaff®, which is the trademark referring to total benzyl ester of hyaluronic acid. Also the above continuous and perforated membrane are made of Hyaff®, in order to have the comparison among supports as significant as possible.

The cells $CaCO_2$ were used at passage 98. The cells were seeded at a density of about $9\times10^3/cm^2$ in DMEM 4.5g of glucose/L containing 20% FBS penicillin/streptomycin, fungizone and non-essential amino acids (1%) in a humidified atmosphere with 95% CO_2. The culture medium was changed every 48 hours.
Other enterocytes were seeded on the following different supports:

- Petri dishes,
- Transwell wells with polycarbonate membranes, and
- Polyurethane membranes (Chronoflex ™).

On the 3rd, 15th, 20th and 40th days of culture, the cells were prepared for assessment of the total proteins and the activity of alkaline phosphates (ALP) according to the following method:

ALP activity: the cells were harvested by scraping in a lysis buffer 2mM Tris-HCl 50 mM mannitol pH 7.2 (1 ml final volume) (with the exception of those seeded on Hyaff 3D) and sonicated in ice. ALP activity of the cellular lysates was determined by spectrophotometry by hydrolysis of the p-nitrophenylphosphate using a Boehringer kit. The total proteins were determined by Lowry's method. The activity present in the cells grown on a scaffold in the form of a non-woven fabric was determined in lysates obtained by sonicating the membrane containing the cells in toto. Values of APL activity are expressed as milliunits per milligram protein mU/mg.

The biochemical differentiation was assessed on the basis of the increase of ALP activity that is a known Enterocyte Differentiation Marker.

Results

In Figure C, the results of ALP activity obtained for $CaCO_2$ cell line grown on

- Petri dishes
- Transwell wells with polycarbonate membranes
- Polyurethane membranes (Chronoflex™)
- a bidimensional continuous membrane, see Figure A
- a bidimensional perforated membrane (Laserskin®);
- a 3-D non-woven Hyaff® matrix, see Figure B.

are shown, where the APL activity is reported after 3, 15, 20 and 40 days for all the above supports respectively.

It should be easily noticed that **the bidimensional continuous and perforated membranes show an unexpectedly great improvement in APL activity with respect to the 3-D non-woven matrix, even when the same raw material is used**. Therefore, contrary to the Examiner's assertion, **the enterocytes do not grow and do not differentiate in 3-D scaffolds in a surprisingly way as in 2-D membranes**. The growing enterocytes on the continuous bidimensional membrane of the invention are shown in Figure D below.

However, the Experiment show that not all the 2-D supports can be suitable for enterocytes. In fact, **the bidimensional continuous and perforated membranes show an unexpectedly great improvement in APL activity also with respect to the Petri dishes, the transwell wells with polycarbonate membranes and the polyurethane membranes (Chronoflex™).**

This confirms with no doubt that morphological differentiation is not a natural development of intestinal seeded cells, as simplicistically concluded by the Examiner, since it has been demonstrated that **only bidimensional continuous and perforated membranes consisting essentially of at least one hyaluronic acid or a derivative thereof can allow to achieve morphologically differentiated enterocytes as confirmed by the presence of microvilli, in order to obtain a biological material suitably *configured* for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus**. The presence of microvilli has been already noticed in the Example given in the Application as filed, where reference is made to Figure 3 showing "*marked differentiation due to the appearance of numerous microvilli on their surfaces*".

It should be also noted that **the APL activity in case of the bidimensional *continuous* membrane is better than the APL activity in case of the bidimensional *perforated* membrane.** Therefore, this is a further surprising and definitely unexpected result achieved by the invention, particularly in view of all the prior art teachings!

**** *** ****

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Date: March 30, 2009

Anna Zanellato

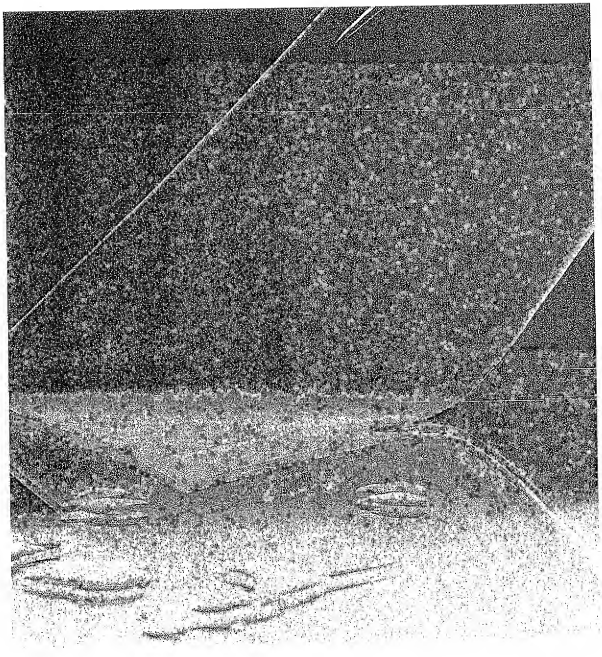

Figure A

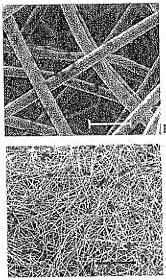

Figure B

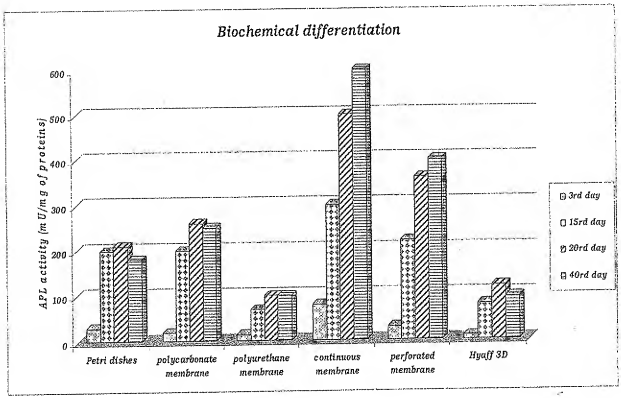

Figure C

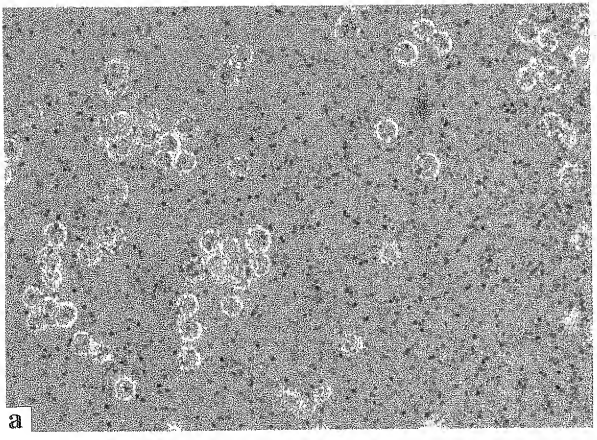

Figure D

(x) Related proceedings appendix

Copy of Board of Patent Appeals and Interference Decision on Appeal of April 16, 2007.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte LANFRANCO CALLEGARO, LUIGI AMBROSIO, and ANNACLAUDIA ESPOSITO

Appeal 2006-3070
Application 09/743,333

ON BRIEF

Before SCHEINER, LINCK, and LEBOVITZ, *Administrative Patent Judges*.

LINCK, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the final rejection of all the pending claims in the above-referenced application, filed February 21, 2001.[1]

Statement of the Case

"The present invention concerns the use of hyaluronic acid or the derivatives thereof for the preparation of a composition to treat ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus." Specification (Spec.) at 1. "The hyaluronic acid or hyaluronic acid derivatives . . . are preferably in the form of gels, guide channels,

[1] The application claims a priority date of July 6, 1998. The real party in interest is Fidia Advanced Biopolymers S.R.L.

sponges, non-woven fabric, threads, continuous or perforated membranes, microspheres, nanospheres, gauzes or associations of the same." *Id.* at 5. A "[b]idimensional or three dimensional matrix containing a hyaluronic acid derivative may be used as support for cellular growth for the preparation of biological material containing suitable cell cultures for regenerating the walls or filling diverticula in the digestive apparatus." *Id.* The working examples disclose the use of "Laserskin® (bidimensional matrix comprising hyaluronic acid esters)" and "Hyaff11 3D (three-dimensional matrix comprising hyaluronic acid esters)." *Id.* at 3-4. Transwell wells, Petri dishes, and polyurethane were used as controls. *Id. See also id.* at 6-7.

Claims 25-32 and 34-44 are pending. They stand rejected under 35 U.S.C. § 112 ¶ 1 ("new matter") and under 35 U.S.C. § 103(a) based on U.S. 5,939,323 (Valentini) and WO 94/17837 (Dorigatti). "The claims of the application stand or fall together." Brief on Appeal (filed November 14, 2005) (Br.) at 3. The single claim argued by Appellants reads:

> 25. A process for the preparation of a biological material for the treatment of ulcers, lesions and diverticula of the digestive and gastrointestinal apparatus, which comprises growing intestinal cells optionally together with fibroblasts, mesenchimal cells, mature cells and/or epithelial cells on a single layer matrix selected from the group consisting of a non-woven fabric and a perforated membrane consisting essentially of at least one hyaluronic acid or a derivative thereof.

We reverse the § 112 ¶ 1 rejection and affirm the § 103(a) rejection.

Issues on Appeal

Both the § 112 and § 103 issues turn on our interpretation of the claim phrase "single layer matrix," a phrase that was added to the claim during prosecution.

Appellants argue this added phrase (1) is "inherently disclosed in the as-filed specification and not does constitute 'new matter;'" and (2) avoids Dorigatti's "multilayer material" and Valentini's "spongy matrices." Supplemental Brief on Appeal (Supp. Br.) at 19, 12-14. The Examiner responds (1) there is no support in the specification for the phrase "single layer matrix" and (2) "if applicants disclosure has 'single layer matrix' inherently disclosed, . . . this limitation would also be inherently present in the spongy matrix of Valentini." Examiner's Answer (Ans.) at 9.

Claim Interpretation

The phrase "single layer matrix" is not defined in the specification. However, the language in the specification, a "[b]idimensional or three dimensional matrix containing a hyaluronic acid derivative may be used as support" (*id.* at 5), suggests a single layer, absent some teaching to the contrary. This is a phrase easier to define by what it is not, i.e., more than one layer, or multilayers affixed to each other in some manner. Thus, a "single layer matrix" excludes multilayers, as described in the Dorigatti reference. Appellants' working examples use both a bidimensional and three dimensional matrix, called Laserskin® and Hyaff®11 3D respectively. There is no teaching or suggestion that either of these materials is multilayered. Thus, each is a "single layer matrix" according to our understanding and may take the form of a sponge or other such non-woven material.

Giving claim 25 its broadest reasonable interpretation, it claims a "process . . . which comprises growing intestinal cells . . . on a single layer matrix [which may be two or three dimensional] . . . consisting of a non-woven fabric [which may be a fabricated sponge] . . . consisting essentially of at least one hyaluronic acid" or derviative.

Alternatively, the single layer matrix can consist of "a perforated membrane . . . of at least one hyaluronic acid" or derivative.

The Prior Art Teachings

Dorigatti discloses "multilayer nonwoven tissue, wherein one of the layers comprises a hyaluronic acid derivative." Dorigatti at 1. The hyaluronic acid derivative layer can be Hyaff® 11. *Id.* at 7. Dorigatti also discloses a "perforated membrane compatible with cell growth on its surface." *Id.* at 2. Dorigatti does not disclose or suggest growing intestinal cells . . . on a single layer matrix," as required by claim 25.

Valentini discloses "three-dimensional biodegradable scaffolds of hyaluronic acid derivatives for tissue reconstruction and repair." Col. 4, ll. 31-33. Valentini's "porous scaffold has interconnected pores that permit cells to grow into the scaffold." Col. 4, ll. 33-35. The porous scaffolds, described by Appellants as "spongy" (Supp. Br. at 14), "can be fabricated to be virtually any shape, size or thickness." Col. 4, ll. 36-37. One skilled in the art would understand Valentini's exemplary scaffolds to be single layer matrices fabricated from hyaluronic acid derivatives, including Hyaff®11. *See, e.g.,* Example 1, col. 8, ll. 20-25. *See also* Ans. at 9.

Valentini's scaffolds "may be used to repair defects and damage in . . . soft tissues such as results from . . . ulcers . . . . Likewise, damage to visceral organs including . . . damage resulting from intestinal cancer or intestinal ulcer may be treated with" Valentini's scaffolds. Col. 7, l. 52 to col. 8, l. 4. "In these instances, the scaffolds can be seeded with cells such as . . . intestinal cells." Col. 8, ll. 4-6.

Analysis

1. The § 112 Written Description Rejection

The specification "as originally filed does not have to provide in haec verba support for the claimed subject matter at issue." *Crown Operations Int'l Ltd. v. Solutia, Inc.*, 289 F.3d 1367, 1376, 62 USPQ2d 1917,1922 (Fed. Cir. 2002). Rather, it need only clearly establish the inventors had possession of the claimed invention at the time the application was filed. In this case, Appellants' working examples, describing their scaffolds as bidimensional Laserskin® and three dimensional Hyaff®11 3D, evidence their timely possession of single layer matrices. While we agree with the Examiner that scaffolds are not necessarily single layered, a multiple layer scaffold requires some type of "stacking" of the individual layers. *See* Ans. at 9. Appellants' examples do not describe or even suggest such a stacking. Thus, we conclude Appellants' examples provide support for the added phrase "single layer matrix."

2. The § 103(a) Rejection

Valentini discloses growing ("seeding") intestinal cells on a single layer matrix consisting of a non-woven fabric (a fabricated spongy matrix) consisting essentially of at least one hyaluronic acid derivative. See the description of Valentini *supra* at p. 3.

Appellants argue the "spongy matrices of Valentini et al. are completely different from the claimed matrices which are in the form of perforated membranes and non woven tissue."[2] Supp. Br. at 14. According to Appellants, a "non-woven tissue of HA is a web composed of fibers joined together by mechanical means or by chemical coagulation. The structure is composed of haphazardly placed fibers. No interconnected pores are

[2] Claim 25 recites "non-woven fabric," not tissue.

present in the structure." *Id.* However, claim 25 is not so limited, either by the claim language itself or by a description in the specification. Again, we conclude a reasonable interpretation of "non-woven fabric" includes the spongy structure of Valentini.

Like Valentini, Dorigatti discloses the growth of cells on non-woven scaffolding. Additionally, Dorigatti discloses using perforated membranes for this purpose. Appellants argue that "any person of ordinary skill in the art aware of the teachings of Dorigatti et al. and Valentini et al. would have tried to grow intestinal cells on the multilayer material disclosed by Dorigatti et al." Supp. Br. at 13. We don't agree. As Valentini teaches a single layer matrix suffices to grow intestinal cells on the matrix, there would be no reason to adopt the more complex system of Dorigatti. Rather, as the Examiner found, the combined teachings would have made the claimed invention obvious. As an alternative to Valentini's spongy matrix to grow intestinal cells, Dorigatti suggests using a perforated membrane for this purpose. *See* Dorigatti at 2. Thus, we conclude Appellants' claimed process, with a matrix either of non-woven fabric or a perforated membrane, would have been obvious to one skilled in the art, in view of the Valentini and Dorigatti references.

Appellants submitted a declaration to overcome the § 103(a) rejection, comparing multilayered matrices with their single layer matrices (Laserskin® and Hyaff® 11 3D). The data do not help Appellants' case, as the closest prior art is that disclosed in Valentini, a single layer matrix of Hyaff® 11 in the form of a spongy structure. *See, e.g.*, Valentini's Example 1.

Conclusion

Appellants' disclosure of single layer matrices in their working examples supports the language "single layer matrix." Thus, we reverse the § 112 ¶ 1 rejection. However, in view of our claim interpretation, we hold the invention of claim 25 would have been obvious in view of Valentini and Dorigatti and thus affirm the § 103(a) rejection of claim 25. As claims 26-32 and 34-44 were not argued separately, we also affirm the rejection of these claims under § 103(a), pursuant to 37 C.F.R. § 41.37(c)(1)(vii).

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a)(1)(iv) (2005).

AFFIRMED

TONI R. SCHEINER
Administrative Patent Judge

NANCY J. LINCK
Administrative Patent Judge

RICHARD M. LEBOVITZ
Administrative Patent Judge

BOARD OF PATENT
APPEALS AND
INTERFERENCES

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